

### Remarks/Arguments

Claims 1-11 and 19-20 are pending in this Application. Claims 12-18 have been withdrawn. In the Office Action mailed on April 3, 2006, the Examiner:

1. rejected Claims 1 and 3-9 under 35 U.S.C. § 102(a) as being anticipated by Awasthi et al. (Proc. Am. Assoc. Cancer. Res. March 2002;43 Abstract #4717);
2. rejected Claims 1 and 3-9 under 35 U.S.C. § 102(b) as being anticipated by Awasthi et al. (Proc. Am. Assoc. Cancer. Res. March 2001;44 Abstract #1517);
3. rejected Claims 1-9 under 35 U.S.C. § 103(a) as being unpatentable over Awasthi et al., (2001) in combination with American Type Culture Collection (Tumor Cell Lines, 2001);
4. rejected Claims 1-11 under 35 U.S.C. § 103(a) as being unpatentable over Awasthi et al., (2001) in view of Sause WT (Chest, 1999; 116:504S-508S); and
5. rejected Claims 19-20 under 35 U.S.C. § 112, first paragraph, for containing subject matter not described in the specification to indicate that the inventors had possession of the claimed invention.

Applicants respectfully address the basis for each of the Examiner's objections and rejections below.

#### ***Claim Rejections – 35 U.S.C. § 102(a)***

On page 2 of the Office Action, the Examiner rejected Claims 1 and 3-9 under 35 U.S.C. § 102(a) as being anticipated by Awasthi et al. (herein "Awasthi 2002"). Applicants resubmit an executed Declaration under 37 § CFR 1.131. The Declaration is signed by one or more Applicants establishing that the Awasthi 2002 reference is describing Applicants' own work. Applicants also provide documentary evidence that accompany the affidavit to show that that subject matter considered prior art under 35 U.S.C. § 102(a) is now disqualified as prior art against this Application for invention. With the evidence provided herewith, Applicants submit that they conceived and reduced to practice in the United States of America the invention as shown and described in the above-identified application prior to the date of March 2002, the date of publication of Awasthi 2002. The evidence represents the reduction to tangible form of the

invention as shown and claimed in the above-identified application. The evidence, provided as EXHIBIT A, is a document that describes methods of the claimed invention. Applicants further submit that prior to March 2002, they disclosed and reported the claimed invention as provided by EXHIBIT A and that they reduced to practice the invention as described and claimed in the above-identified application in the United States of America prior to March 2002.

***Claim Rejections – 35 U.S.C. § 102(b)***

On page 4 of the Office Action, the Examiner rejected Claims 1 and 3-9 under 35 U.S.C. § 102(b) as being anticipated by Awasthi et al. (herein “Awasthi 2001”). Applicants respectfully submit amended Claim 1, amended to include a method of “treating one or more cells undergoing uncontrolled growth comprising the step of contacting the one or more cells with an antibody to ralA binding protein1, wherein the contact is cytotoxic to the one or more cells in the absence of an additional agent and wherein the antibody blocks the function of the ralA binding protein1” [Emphasis indicating amended text] Support for amended Claim 1 may be found throughout the specification, see, e.g., para. [0009]. Applicant respectfully points out that Awasthi 2001 does not disclose or suggest amended Claim 1, including wherein the antibody blocks the function of ralA binding protein1. Rather, Awasthi 2001 discloses that “antibodies markedly augment the cytotoxicity of doxorubicin,” which is not equivalent to antibodies themselves being cytotoxic. The Examiner asserts that Awasthi 2001 teaches administrations of anti-RLIP76 alone to SCLC and NSCLC cells results in DNA laddering; however, Applicants submit that this is not conclusive of cytotoxicity, since some DNA laddering may always be found in cancer-like cells such as SCLC and NSCLC cells, which is quite clear since Awasthi 2001 further described that it is only when doxorubicin in combination with an antibody are applied to such cells that “DNA laddering was. . . significantly increased.” The Examiner further asserts that Awasthi 2001 “teaches that the anti-RLIP76 antibodies are useful as a therapeutic modality.” However, Applicants submit that no such thing is taught by Awasthi, but merely speculated to “suggest that anti-RLIP antibodies may be useful as a therapeutic modality.” Applicants point out that speculation is not a teaching with any predictability and cannot be used as evidence for a teaching of the claimed invention. As such, Applicants submit that Awasthi 2001 does not teach each and every element of amended Claim 1. Claim 1 is, therefore, not anticipated by Awasthi

2001. Entry and allowance of amended Claim 1 and its dependents claims are respectfully requested.

***Claim Rejections – 35 U.S.C. § 103(a)***

On page 5 of the Office Action, the Examiner rejected Claims 1-9 under 35 U.S.C. § 103(a) as being unpatentable over Awasthi 2001 in combination with American Type Culture Collection (herein “ATTC”). For the reasons set forth above, Applicants submit that Claims 1-9 are not anticipated by Awasthi 2001. Combining Awasthi 2001 with ATTC, which is merely a collection of cell types, does not overcome the fundamental failure of Awasthi 2001 to anticipate each and every element of independent and amended Claim 1 or amended Claim 1 on its whole. Neither ATTC nor Awasthi 2001 suggest or teach all elements of the claimed invention or the claimed invention as a whole. In addition, ATTC does not suggest or teach any portion of amended Claim 1 that Awasthi 2001 fails to teach, such as treating one or more cells undergoing uncontrolled growth or contacting the one or more cells with an antibody to ralA binding protein<sup>1</sup> or wherein contact is cytotoxic to the one or more cells in the absence of an additional agent or wherein the antibody blocks the function of the ralA binding protein<sup>1</sup>.” Thus, combining ATTC with Awasthi 2001 does not overcome the deficiencies of Awasthi 2001 nor do the combination teach Applicants claimed invention on its whole. Applicants submit that the lack of teaching in either Awasthi 2001 or ATTC mean that there is no suggestion or motivation to combine reference teachings. Furthermore, no person of ordinary skill would have reason to combine ATTC with Awasthi et al. in order to arrive at amended Claim 1 nor can there be found any teaching or suggestion in Awasthi 2001 or in ATCC to modify or combine references in such a way that would resemble Applicants’ invention as claimed in amended Claim 1. Without such suggestion or motivation, there is no reasonable expectation of success. Accordingly, Applicants submit that amended Claim 1 and its dependents claims are patentably distinct from the cited art and respectfully request entry and allowance of these claims.

On page 7 of the Office Action, the Examiner rejected Claims 1-11 under 35 U.S.C. § 103(a) as being unpatentable over Awasthi 2001 in view of Sause. For the reasons set forth above, Applicants submit that Claims 1-11 are not anticipated by Awasthi 2001. Accordingly, Awasthi does not teach the claimed invention as amended. Combining Awasthi 2001 with Sause,

does not overcome the failure of Awasthi 2001 to teach amended Claim 1. The Examiner asserts that “it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to treat one or more cells undergoing uncontrolled growth. One of skill in the art would have been motivated to do so because each of the therapeutics had been individually taught in the prior art to be successful at treating cells undergoing uncontrolled growth. . . one of ordinary skill in the art would have reasonably expected that adding RLIP76 antibodies in combination with radiation therapy, one would achieve an enhanced method of treating cells undergoing uncontrolled growth.”

Applicants point out that amended Claim 1 does not teach adding RLIP in combination with radiation therapy. Accordingly, Applicants submit that combining Sause, a reference merely disclosing some of the benefits of administering radiation therapy in patients with locally, does not overcome the failures of Awasthi 2001, a reference that also does not teach amended Claim 1. The Examiner may combine reference teachings when each disclose one or more portions of a claimed invention; however, Applicants see no portion of amended Claim 1 that is taught by Sause, such as contacting the one or more cells with an antibody to ralA binding protein1 or wherein contact is cytotoxic to the one or more cells in the absence of an additional agent or wherein the antibody blocks the function of the ralA binding protein1, which are the relevant portions of amended Claim 1. Accordingly, combining Sause with Awasthi 2001 does not meet the analysis set forth in In re Kerkhoven because Sause does not teach any portion of the “composition” of amended Claim 1 nor does its teachings flow logically from amended Claim 1. As such, Applicants submit that no person of ordinary skill would have reason to combine such references to provide for Applicants’ invention as claimed in amended Claim 1. Both Awasthi 2001 and Sause are each unpredictable with respect to amended Claim 1 and some degree of predictability is required in the references for a showing of obviousness. Without any predictability, there is no reasonable expectation of success. Thus, Applicants submit that amended Claim 1 and its dependents are patentably distinct from the cited art and respectfully request entry and allowance of these claims.

***Claim Rejections – 35 U.S.C. § 112, first paragraph***

On page 10 of the Office Action, the Examiner rejected Claims 19-20 under 35 U.S.C. § 112, first paragraph, for not describing subject matter as provided in the specification.

Applicants respectfully submit amended Claim 19, amended in accordance with the specification and believed to overcome the rejection under 35 U.S.C. § 112, first paragraph. Applicants further submit that amended Claim 19 is not taught by either Chen et al., Awasthi 2001 or the combination and request the Examiner point to such a specific teaching should it exist.

### Conclusion

In light of the amendments, remarks and arguments presented with this Amendment, Applicants respectfully submit that the pending and amended claims are in condition for allowance. Accordingly, favorable consideration for and allowance of such claims are respectfully requested.

A Request for Continued Examination is filed concurrently with this paper and with the appropriate fees along with a petition and appropriate fees for a three-month extension of time. No additional fees are believed due with this Amendment. If this is incorrect, the Commissioner is authorized to charge those additional fees, other than the issue fee, that may be required by this paper to Deposit Account No. 07-0153.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

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Respectfully submitted,

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